Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Claims 119-131 are pending in this application and are rejected on various grounds. Claims 119-123 have been amended with a functional recitation. Further, all pending claims have been amended to remove references to "Figures". The rejections to the presently pending claims are respectfully traversed.

Priority

Applicants rely on the 'Mixed lymphocyte reaction' assay for patentable utility in this case. This utility was first disclosed in International Application PCT/US00/05841, filed March 2, 2000, priority for which has been claimed in this application. Further, the PRO1346 sequence and the nucleic acid encoding it was first disclosed in U.S. Provisional application 60/097661, filed 8/24/1998, (as SEQ ID NO: 2 and 1), priority for which has also been claimed in this application. Hence, the present application is at least entitled to an effective filing date of **March 2, 2000.**

Information disclosure Statement

References were required in proper format. Applicants have filed a Supplemental IDS with reference to the author and date of deposit.

Specification

A. The disclosure was objected to by the Examiner as containing "embedded hyperlink and/or other form of browser-executable code." The foregoing amendment to the specification which deleted all embedded hyperlinks, is believed to overcome the present objections.

B. The title of the invention was objected to. Applicants have amended the title to better describe the claimed invention.

Accordingly, Applicants believe that all objections to the specification has been overcome.

Claim Objections

Applicants have amended the claims to remove references to Figures according to the Examiner's suggestion.

Claim Rejections – 35 USC § 101

Claims 119-131 are rejected under 35 U.S.C. §101 allegedly because "the instant application does not disclose a specific and substantial biological role of this protein or its significance." For the reasons outlined below, Applicants respectfully disagree.

Utility Standard

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance with the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: **"If the (A)pplicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion**

would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the Applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

To overcome the presumption of truth based on an assertion of utility by the Applicant, the Examiner must establish that **it is more likely than not** that one of ordinary skill in the art would doubt the truth of the statement of utility. **Absolute predictability is not a requirement.** Only after the Examiner has made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the applicant. The issue will then be decided on the totality of evidence.

Further, the legal standard with respect to *in vitro* or animal model data providing pharmacological activity has been commented on in *Cross v. Iizuka*, 753 F.2nd 1040, 1051, 224 USPQ 739, 747-48 (Fed. Cir. 1985):

> "We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the compound in question. Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vitro* utility."

Furthermore, M.P.E.P. 2107.03 (III) states that:

> "If reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process."

Thus, the legal standard accepts that *in vitro* or animal model data is acceptable utility as long as the data is "reasonably correlated" to the pharmacological utility described.

Arguments

PRO1346 has utility

Without acquiescing to the propriety of this rejection, solely in the interest of expediting prosecution in this case, Applicants submit a declaration and supportive references from the art to support the immunostimulant activity of PRO1346.

Applicants submit a declaration by Sherman Fong, Ph.D. of Genentech, Inc., an expert in the field of Immunology and co-inventor of the present application, to show that there are specific immune stimulant utilities for compounds identified by an MLR assay. The Declaration explains how the MLR reaction was performed in the instant application using peripheral blood mononuclear cells (PBMCs), which contain responder T-cells, and allogenic, pre-treated (irradiated) PBMCs, which predominantly contained dendritic cells. As Dr. Fong emphasizes, immunostimulants are important and are very desirable in the treatment of cancer and in enhancing the effectiveness of previously identified treatments for cancer. Supportive evidence also comes from teachings in the art like Steinman *et al.* (Exhibit B) who states that "...**medicine needs therapies that enhance immunity or resistance to infections and tumors**. (page 1, column 1, line 7; emphasis added)". Further teachings like Peterson *et al.* (Exhibit D) show that, recently, the immune stimulant IL-12, was successfully used in a cancer vaccine trial to treat melanoma. Further, as Dr. Fong explains regarding the IL-12 melanoma trial:

> "Due to the immune stimulatory effect of IL-12, **the treatment provided superior results** in comparison to earlier work, where the patients' own dendritic cells were prepared from peripheral blood mononuclear cells (PBMCs) treated with antigens, then cultured *in vitro* and returned to the patient to stimulate anti-cancer response" (Emphasis added).

Further, Dr. Fong's declaration clearly states that:

> "A PRO polypeptide shown to stimulate T-cell proliferation in the MLR assay of the present invention with an activity of at least 180% of the control is expected to have the type of activity exhibited by IL-12 and would find practical utility as an immune stimulant".

Accordingly, the positive results obtained in this assay clearly establish the immunostimulant

utility for the polypeptides claimed in the present application, and the specification, in turn, enables one skilled in the art to use the compounds for the asserted purpose.

By the foregoing arguments and supportive evidence, Applicants have established that the MLR reaction is a generally recognized assay to assess immunostimulatory activity. Thus, besides the previously asserted immunostimulatory uses of PRO 1346, for example, in the treatment of viral infections like HIV or Epstein Barr viral infections, Applicants assert other utilities in the treatment of cancers like melanoma. Further, since the legal standard accepts *in vitro* as acceptable utility and the data is "reasonably correlated" to the pharmacological utility based on the discussions above, a valid case for utility has been made and would be considered credible by a person of ordinary skill in the art. For the same reason, one skilled in the art at the priority date of the present application would have reasonably accepted this utility.

In view of the foregoing arguments and submitted evidence, the Examiner is respectfully requested to reconsider and withdraw the present rejections.

Claim Rejections - 35 USC § 112, first paragraph -enablement

Claims 119-131 are rejected under 35 U.S.C. §112, first paragraph for failing to adequately teach how to use the instant invention.

As discussed above, Applicants submit that PRO1346 has utility based on the MLR assay as an immunostimulator. These utilities would readily be understood, appreciated and accepted by those skilled in the art at its effective filing date, based on the general knowledge in the art and the disclosure of the present application. therefore, Applicants request reconsideration and withdrawal of this rejection.

Claims 119-131 are rejected under 35 U.S.C. §112, first paragraph for lack of enablement. The Examiner required that "elements required for practicing a claimed invention must be known and readily available to the public or obtainable by a repeatable method set forth in the specification."

Applicants submit amendments to the specification regarding the ATCC deposit incorporating the requisite assurances that "all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent." Accordingly, Applicants request that this rejection be withdrawn.

Claims 119-131 are also rejected under 35 U.S.C. 112, first paragraph because, according to Examiner, "the specification, while being enabling for SEQ ID NO: 313 and 314, does not reasonably provide enablement for polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity to SEQ ID NO:314, ATCC No 203128, its extracellular domain or fusion proteins. Applicants respectfully traverse this rejection.

Again, as discussed above, Applicants submit that PRO1346 has utility based on the MLR assay as an immunostimulator and the pending claims recite this functional feature for the PRO1346 polypeptides. The pending claims are drawn to a genus of polypeptides defined both by sequence and functional identity. It would have been obvious to one skilled in the art at the effective priority date, in view of Applicant's possession of the PRO1346 sequence (SEQ ID NO: 314), based on the general knowledge in the art, and the disclosure of the present application, how to make the obvious variations and adaptations of SEQ ID NO: 314 as well, at the time of filing. Therefore, Applicants request reconsideration and withdrawal of this rejection.

Claim Rejections - 35 USC § 112, first paragraph -written description

Claims 119-131 are rejected under 35 U.S.C. 112, first paragraph because allegedly, the subject matter was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time of filing.

Again, specific utility has now been asserted for the present invention and pending claims recite a functional limitation reciting "wherein said polypeptide is an immunostimulant" for PRO1346 polypeptides. Since the claims are drawn to a genus of polypeptides defined both by sequence and functional identity, one skilled in the art knew at the effective priority date of this application, that the Applicants possessed the claimed sequences.

Hence, Applicants request that the present rejection to the present claims be reconsidered and withdrawn.

Claim Rejections – 35 USC § 112, second paragraph

Claims 119-131 were rejected under 35 U.S.C. §112, second paragraph for being vague and indefinite. The Examiner alleges that the protein identified as PRO1346 is disclosed as a

soluble protein (protease)and accordingly, claims that recite an "extracellular domain" is indefinite as the art does not recognize soluble proteins as having such domains. Applicants respectfully traverse this rejection.

Applicants submit that at least on page 205, lines 30-34, the present protein (NL7 polypeptide) is disclosed as having a transmembrane domain tentatively identified as extending from about amino acid position 31 to 50 in the NL7 amino acid sequence (Figure 228, SEQ IN NO:314). Further, part (d) of the claim has been deleted for clarity. Accordingly, Applicants submit that the phrase "the extracellular domain" is definite and respectfully request that this rejection be withdrawn.

Claim Rejections – 35 USC § 102

A. Claims 119-124 are rejected under 35 U.S.C. §102(b) as being anticipated by Baker (WO99/63088- published December 1999).

As discussed under the section of priority, the PRO1346 sequence and its encoding nucleic acid was first disclosed in U.S. Provisional application 60/097661, **filed 8/24/1998**, (as SEQ ID NO: 2 and 1), priority for which has been claimed in the instant application. Further, the cited Baker publication is the PCT/US99/12252 application, to which priority has also been claimed in the instant application. Therefore, Baker *et al.* is not prior art and Applicants request that this rejection be withdrawn.

Art of interest: Fernandez (WO00/61754- dated October 2000).

Based on the effective priority date of **March 2, 2000** for this application, Fernandez is not prior art. Hence, this rejection is moot.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-2730P1C23). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: September 9, 2004

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